REMARKS

Claims 3, 9-13 and 16-18 and 22 remain in the case. Claims 9 to 13 are withdrawn from consideration pending allowance of product claims.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 3 has been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to point out and distinctly claim the subject matter which the Applicant regards as the invention. The Examiner objects to the terms "activated Cry" because she is of opinion that it is not clear how the Cry polypeptide is activated. The Examiner suggests that since the specification indicates that the polypeptide at issue is "trypsin-activated", the claim should be so limited.

The objected terminology was removed from the claim and replaced by the term polypeptide fragment. Applicant wishes to submit that the term "activated Cry" had been used simply to reflect the fact that what is claimed is a crystal protein without its pro-segment. The crystal protein that the Applicant had isolated from *Bacillus thuringiensis* was inactive (i.e. it had no observed cytotoxic activity) and had a length of 742 amino acids (see Figure 5). It is only when the pro-segment of this protein was removed that the crystal protein's active fragment was revealed, namely the C-terminal 492 amino acids fragment. Now that the nature of this active fragment is known, it can be produced by any means known in the art including routine recombinant techniques or enzymatic cleavage with enzymes having appropriate proteolytic activity including trypsin. The means by which the claimed crystal protein fragment was first obtained is irrelevant to the nature of the claimed invention. The claimed invention is a polypeptide that is appropriately defined by structure. The claim does not encompass "all possible activated Cry polypeptides" but only Cry 31Aa polypeptide fragments that satisfy the recited structure limitations namely polypeptides that comprise a sequence having at least 97% identity with SEQ ID NO: 8.

The Examiner requests that the term "exhibiting" be replaced by the term "having" in claim 3. Claim 3 was amended accordingly.

The Examiner is of opinion that the claim should further identify the nature of the claimed Cry polypeptide. The Examiner suggests that SEQ ID NO: 8 be

identified as Cry31Aa2 and that SEQ ID NO: 18 be identified as Cry31Aa1. The Applicant agrees to identify the sequences as follows.

SEQ ID NO: 8

The Examiner suggests that the Cry31Aa2 name be used to designate SEQ ID NO: 8. This sequence is designated by the appropriate terminology Cry31Aa2 polypeptide fragment.

Claim 3 was also amended to specify that the claimed polypeptide which is any peptide having at least 97% identity with the Cry31Aa2 fragment as set forth in SEQ ID NO: 8 is a Cry31Aa polypeptide. The terminology "Cry31Aa2" does not appropriately designate all polypeptides recited in claim 3 for the following nomenclature reasons.

The nomenclature for *Bacillus thuringiensis* crystal proteins is well codified (see Crickmore et al., Microbiol. Mol. Biol. Rev. 1998, 62(3): 807-813, a copy of which is enclosed).

The name given to any particular *Bacillus thuringiensis* crystal protein ("Cry") has four ranks: a primary rank (an Arabic number; e.g. "31"), a secondary rank (an uppercase letter; e.g. "A"), a tertiary rank (a lowercase letter; e.g. "a"), and a quaternary rank (another Arabic number; e.g. "2") (hence Cry31Aa2 for the crystal protein isolated by the Applicant).

Any Cry protein natural isolate would be specified with a new quaternary rank (Cry31Aa3, Cry31Aa4, etc...). Thus, closely related independently isolated Cry proteins, and even independently isolated Cry proteins with identical sequences will receive separate quaternary ranks.

Variants of Cry31Aa2 (obtained through recombinant DNA as opposed to natural isolates) would be indicated with a superscript (e.g. Cry31Aa2^{n}).

Hence, since, as indicated above, instant claim 3 recites not only the isolated Cry31Aa2 polypeptide fragment of SEQ ID NO:8 but also any polypeptide having at least 97% identity with this Cry31Aa2 polypeptide fragment, not all members of the claimed polypeptides group can be properly designated a Cry31Aa2 polypeptide fragment. In fact, only the specific polypeptide of SEQ ID NO:8 can be

so designated. It is believed however that the more general terminology Cry31Aa would adequately designate all polypeptides covered by the claim.

SEQ ID NO: 18

As previously indicated, claim 3 specifically excludes the polypeptide fragment corresponding to amino acids at positions 232 to 723 of SEQ ID NO: 18 since this sequence is known from the prior art. It is a Cry31Aa1 fragment. As we understand it, when a specific sequence is provided in a claim, there is no requirement for providing any additional description of the sequence. Nevertheless, in order to accelerate prosecution of this case, claim 3 was amended to specify that SEQ ID NO: 18 is a fragment of Cry31Aa1.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraw her rejection of claim 3 under 35 U.S.C. § 112, second paragraph.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 3 and 16-22 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement because of their recital of "activated Cry polypeptide" while the specification discusses only "trypsin-activated" Cry polypeptide. As indicated above, claim 3 was amended to recite a Cry31Aa polypeptide fragment.

The Applicant again submits that the claim wording properly defines the nature of the recited polypeptide. The claim does not encompass "all possible activated Cry polypeptides" but only Cry31Aa polypeptide fragments that satisfy the structure limitations in the claim namely polypeptide fragments that comprise a sequence having at least 97% identity with SEQ ID NO: 8. As previously indicated, the claim however expressly excludes Cry31Aa1 which is known from the prior art.

The Examiner also rejects claim 3 because it "*refers to all "human cancer cells" where the specification, see Table 2, page 32 provides only support to*

human: uterus, blood, lung, liver and colon cancer" (see page four of the current Office Action).

Claim 3's amendment specifying that it recites a polypeptide having cytotoxicity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells is believed to overcome this objection. Support for this amendment may be found at Table 2 at page 32 of the application.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraw her rejection of claims 3 and 16-22 under 35 U.S.C. § 112, first paragraph.

The rejections of the claims are believed to have been overcome by the present remarks. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

Authorization is hereby given to charge deposit account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,
AGRICULTURE AGROLIMENTAIRE
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